Neonatal Lupus Erythematosus Presenting as Atypical Targetoid-like Lesions Involving Genitals and Soles of Feet Following Brief Sun Exposure

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A Focus on Children

Message from Andrew Krakowski, MD

Pediatric dermatology is and always will be a field that relies on innovation. Because most medical developments are, at least initially, directed at the adult population, we as pediatric dermatologists must be uniquely resourceful in our efforts to adapt existing and emerging treatment strategies to the particular challenges facing our young patients. From the specific risks of prematurity to the potential exposures facing an unvaccinated school-age child to the psychosocial complexities underlying any treatment plan aimed at teenagers, this "in the trenches" specialty of dermatology demands clinical flexibility and a patient-centered approach.

To help highlight and advance these considerations, I am honored to introduce to you the newly created Pediatric Dermatology Special Section of The Journal of Clinical and Aesthetic Dermatology. *Beginning in 2013, this new section will be phased in as a regular feature and will focus attention on the many developments that enhance our understanding of how to better manage the skin of infants,*

Abstract

Neonatal lupus erythematosus is a rare autoimmune disease caused by transplacental passage of maternal autoantibodies against Ro/SS-A, La/SS-B, and U1-ribonucleoprotein. The clinical spectrum of neonatal lupus erythematosus comprises cutaneous, cardiac, and systemic abnormalities. Typical cutaneous manifestations include annular erythematous plaques with or without fine scale predominately on the scalp, neck, or face and less commonly on the trunk and extremities. The authors describe the case of a two-month-old male child who developed atypical, targetoid-like lesions involving the genitals and soles of the feet after brief sun exposure and was subsequently diagnosed with neonatal lupus erythematosus.

Introduction

Neonatal lupus erythematosus (NLE) is an autoimmune disease caused by transplacental passage of maternal autoantibodies against Ro/SS-A, La/SS-B, and, less commonly, U1-ribonucleoprotein (U1-RNP).[1] It is a rare condition and estimated to occur in 1 in 20,000 live births.[2] NLE is seen in less than 2.5 percent of infants born to mothers with these autoantibodies, and a great majority of mothers are asymptomatic at the time of delivery.[3,4] The course is generally benign and self-limited; however, NLE may be associated with serious sequelae.[1]

The authors describe the case of a two-month-old male child who developed atypical, targetoid-like lesions involving the genitals and soles of the feet after brief sun exposure and was subsequently diagnosed with NLE.

Case Report

A two-month-old male child

children, adolescents, and young adults. More specifically, we will expand the knowledge of our readers through the publication of timely manuscripts that examine effective diagnostic and treatment strategies for children's skin conditions, and we will encourage collaborations and dialogues with experts from within the subspecialty of pediatric dermatology.

I should point out that our new section aims to be more than a simple repository of pediatric dermatology articles. Instead, we hope to provide a dynamic, evolving, primary source of information for the truly international clinical and aesthetic dermatology communities. We value research that both addresses important gaps in existing approaches to clinical management and creates new perspectives that move beyond existing theories and arguments. We look forward to offering the many gifted and talented minds of the pediatric dermatology community a forum in which to present, discuss, and debate the pressing issues of the day. I encourage you to participate as a reader, as a reviewer, and as an author.

Consideration for inclusion in the Pediatric Dermatology section will be given to child-focused manuscripts that fit into existing categories for Clinical Trials, Clinical Science, New Medications/Instruments, Procedural/Surgical Techniques, or Research Letters as described in the Authors' section. Preference for publication will be given to concise manuscripts whose results and conclusions are adequately supported by data and rigorous statistical analysis. A desire to be considered for this new section should be indicated by the authors at the time of manuscript submission.

Within this inaugural issue is a featured pediatric dermatology contribution from Dr. Shehla Admani at Rady Children's Hospital, San Diego. In her clinical review of neonatal lupus, Dr. Admani highlights an atypical morphological and anatomically distributed presentation of this "not-as-rare-as-we-think" condition and the aggressive topical treatment strategy that was employed to successfully prevent long-term sequelae. She then briefly, but elegantly, discusses the topic from a pediatric perspective and offers several clinical pearls regarding "head-to-toe" management of these patients.

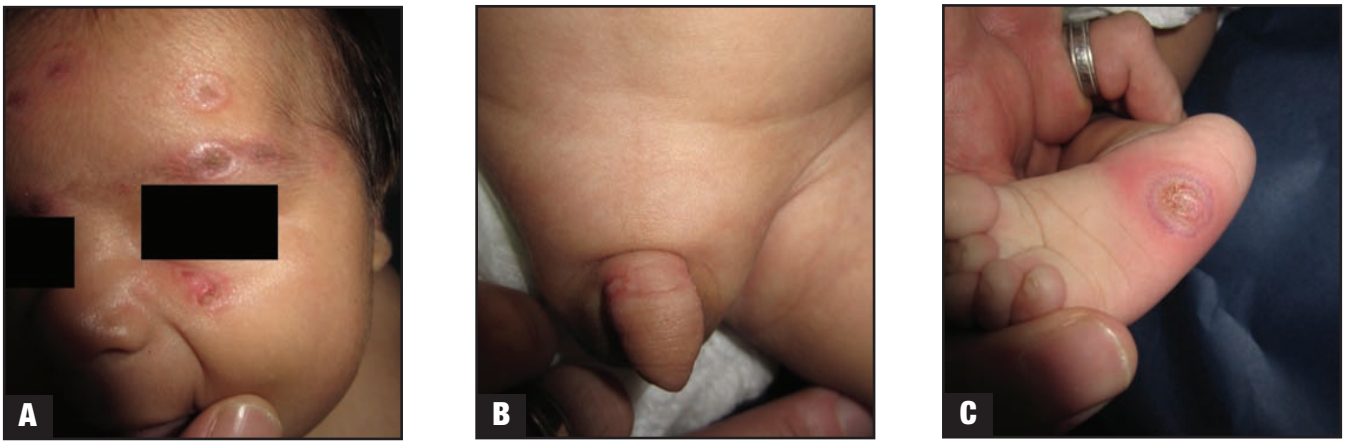
We are delighted to have the opportunity to work with you as an active and inquisitive member of the Green Journal's community at large. We hope that you enjoy the new Pediatric Dermatology section and greatly encourage your feedback and submissions.

Have a wonderful and prosperous 2013!

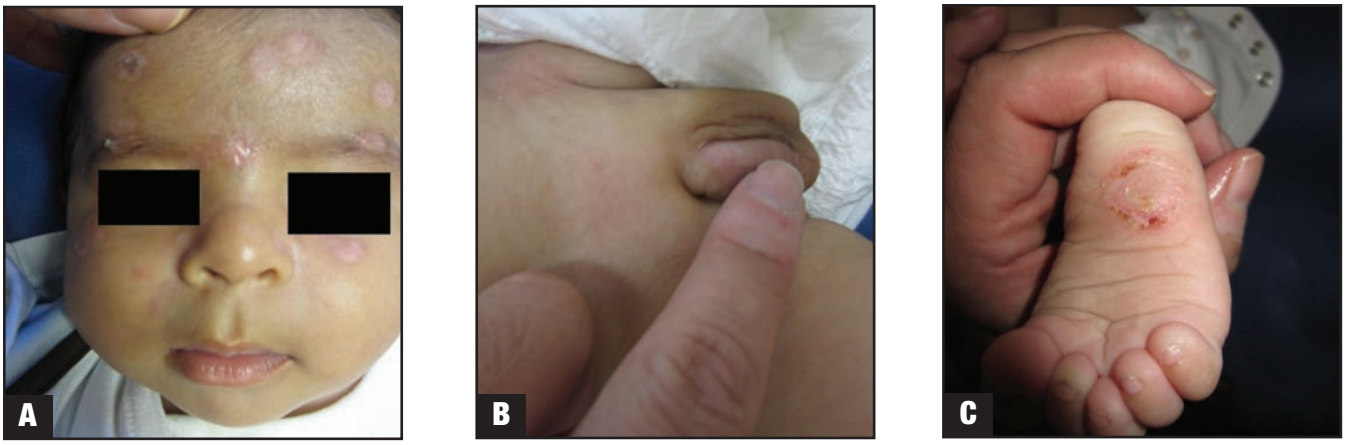
presented to a pediatric dermatology clinic with a three-week history of a rash that started on his forehead and was soon thereafter noted on his groin, sole of the right foot, and trunk. The rash initially appeared three days after a family picnic during which time the mother noted sun exposure to the infant's face and also recalled full-body sun exposure as a consequence of changing the patient's diaper outdoors. The patient's primary care physician had treated empirically with a trial of antifungal cream, which resulted in no improvement of the rash. The patient seemed otherwise in good health with no significant past medical or surgical history. Of note, the patient's mother had a history of active systemic lupus erythematosus (SLE) and rheumatoid arthritis.

On physical exam, the patient was noted to have numerous pink, round, targetoid-like papules and plaques with central hemorrhagic crust on his face (Figure 1). He also had several scattered, eroded, pink, round papules and plaques on his abdomen, right inguinal region, left lower extremity, and penis. In addition, the patient had a larger, round, eroded plaque with central hemorrhagic crust on the sole of his right foot.

Given the mother's own medical history and the subsequent concern for NLE, the patient had an urgent in-clinic electrocardiogram (EKG) performed, which was read by pediatric cardiology and found to be within normal limits. Laboratory evaluation revealed a positive SS-A (>8), negative SS-B, and negative U1-RNP. Further testing showed a complete blood count within normal limits, aspartate aminotransferase (AST) 131 (ref 20-60), alanine aminotransferase (ALT) 168 (ref 5-48), and alkaline phosphatase 383 (ref 110-300). The patient's AST and



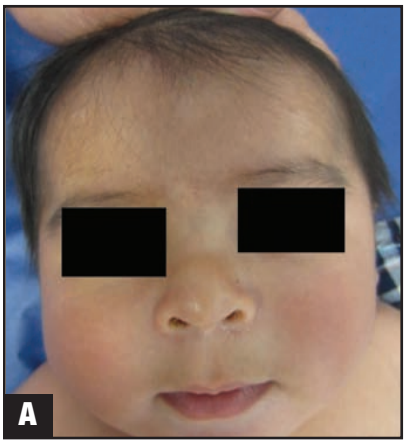
Figures 1A–1C. Face with numerous pink, round, targetoid-like papules and plaques with central hemorrhagic crust (A). Round, pink, partially eroded papule on shaft of penis (B). Sole of right foot with 3cm pink, violaceous, round, eroded plaque with central hemorrhagic crust (C).

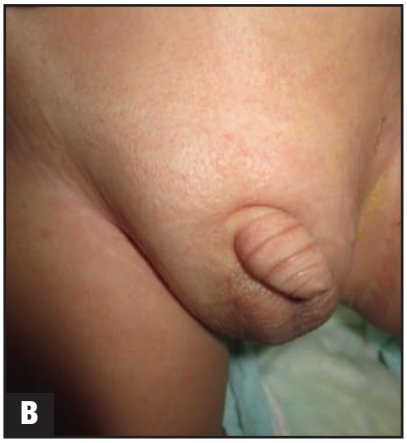


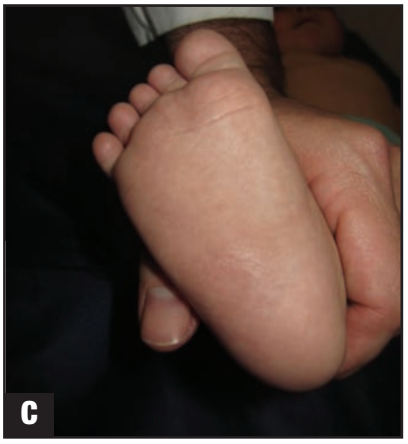
Figures 2A–2C. At two-week follow-up with aggressive topical steroid application, patient showed no evidence of further ulceration (A). Well-healed lesion on shaft of penis with only residual erythema remaining (B). Lesion on sole of foot much improved after two weeks of fluocinonide treatment (C).

ALT continued to trend up to 319 and 506, respectively. He was referred to pediatric gastroenterology by his pediatrician and a liver biopsy was performed, which showed only mixed portal and lobular inflammation and no evidence of autoimmune hepatitis. One month later, AST and ALT were trending down at 116 and 122, respectively; the patient has further gastroenterology follow-up pending. Further cardiac work-up included a chest x-ray, which showed no cardiac abnormality and an echocardiogram, which showed a patent foramen ovale, mild right ventricular hypertrophy, and no other intracardiac abnormalities. The patient has now been discharged from cardiology clinic.

To help minimize scarring from the already-eroding lesions, the patient was prescribed fluocinonide 0.05% ointment twice daily for two weeks straight to all lesions (the mother was specifically instructed to avoid use around the eyes). Coupled with strict sun protection and sun avoidance, this aggressive topical regimen led to significant improvement of the skin lesions, and no further ulceration was noted at the two-week follow-up appointment (Figure 2). Consequently, the patient was tapered to desonide 0.05% ointment twice daily for two weeks straight to







Figures 3A–3C. At three-month follow-up, the patient had complete resolution of all lesions on the face (A). Complete resolution of genital lesion (B). Resolved lesion on sole of foot with only slight hyperpigmentation remaining (C).

all lesions with total resolution noted at the three-month follow-up appointment (Figure 3). The topical medication was then discontinued, and the patient has remained symptom- and sign-free to date.

Discussion

The clinical spectrum of NLE comprises cutaneous, cardiac, and systemic abnormalities. The most common clinical manifestation of NLE is a cutaneous eruption consisting of annular erythematous plaques with or without fine scale predominately on the scalp, neck, or face and less commonly on the trunk and extremities.[4,5] The skin lesions in NLE patients are generally more similar to those seen in subacute lupus erythematosus, rather than the classic "malar rash" of SLE.[6,7] Another typical presentation of NLE is periorbital erythema, often referred to as "raccoon eye" or "owl eye."[4,8] Urticarial, desquamative, ulcerative, crusted, and bullous lesions have also been described.[9–11]

The cutaneous findings of NLE can be present at birth or appear in the first few weeks of life.[12] The pathogenesis is related to the cytotoxic effect of NLE sera on keratinocytes and this effect is further enhanced with ultraviolet light exposure.[13–15] Although the rash typically occurs in a photoexposed distribution, ultraviolet light exposure is not a requirement for the development of cutaneous NLE.[16] The rash of NLE generally resolves by six months of age, at around the same time the maternal autoantibodies are cleared from the infant's circulation.[12] Treatment consists of avoidance of sun exposure, sunscreen, and topical corticosteroids.[17]

Cardiac involvement is the most serious concern in NLE and may consist of conduction abnormalities (first-, second-, and third-degree heart block) and/or cardiomyopathy.[1] Congenital heart block in the absence of structural cardiac abnormalities is most commonly caused by NLE and more specifically maternal autoantibodies against Ro/SS-A and/or La/SS-B.[18,19] Congenital heart block can present as bradycardia and third-degree heart block, once established, is usually irreversible.[5,20] Cardiac involvement has a 15- to 30-percent mortality rate and requires regular monitoring of cardiac function and, in some cases, a pacemaker.[18] Hepatobiliary and hematological manifestations include elevated liver enzymes, conjugated hyperbilirubinemia, mild hepatomegaly, neutropenia, and thrombocytopenia.[9] These are usually self-limited; however, severe cases may require systemic corticosteroids, intravenous immunoglobulin (IVIG), and/or immunosuppressive agents.[17,21] Although the patient in our case had a noted transaminitis, liver biopsy showed no evidence of autoimmune hepatitis and the patient had down-trending AST and ALT; the decision was made to hold off on any systemic therapy and continue to follow labs until they normalize.

Atypical presentations of NLE can pose a diagnostic challenge for many physicians. Given the potentially life-threatening associated abnormalities, NLE should be considered in neonates presenting with atypical rash, and, when appropriate, a work-up that includes EKG and serological evaluation should be initiated. Prior cases of NLE with genital involvement

have been reported; however, these were not thought to be secondary to sun exposure.[22] The patient described in this case demonstrates a direct temporal association with sun exposure to the genital area and development of NLE lesions and highlights a unique presentation of NLE.

References

1. Hon KL, Leung AK. Neonatal lupus erythematosus. *Autoimmune Dis.* 2012;2012:301274.
2. Lee LA. Neonatal lupus erythematosus. *J Invest Dermatol.* 1993;100:9–13.
3. Zuppa AA, Fracchiolla A, Coat F, et al. Infants born to mothers with anti-SSA/Ro autoantibodies: neonatal outcome and follow-up. *Clin Pediatr (Phila).* 2008;47(3):231–236.
4. Wisuthsarewong W, Soongswang J, Chantorn R. Neonatal lupus erythematosus: clinical character, investigation, and outcome. *Pediatr Dermatol.* 2011;28(2):115–121.
5. Lee LA. Cutaneous lupus in infancy and childhood. *Lupus.* 2010;19(9):1112–1117.
6. Neiman AR, Lee LA, Weston WL, Buyon JP. Cutaneous manifestations of neonatal lupus without heart block: characteristics of mothers and children enrolled in a national registry. *J Pediatr.* 2000;137(5): 674–680.
7. Cimaz R, Spence DL, Hornberger L, Silverman ED. Incidence and spectrum of neonatal lupus erythematosus: a prospective study of infants born to mothers with anti-Ro autoantibodies. *J Pediatr.* 2003;142:678–683.
8. Perez MF, de Torres ME, Buján MM, et al. Neonatal lupus erythematosus: a report of four cases. *Anais Brasileiros de Dermatologia.* 2011;86(2):347–351.
9. Silverman E, Jaeggi E. Non-cardiac manifestations of neonatal lupus erythematosus. *Scand J Immunol.* 2010;72(3):223–225.
10. Penate Y, Lujan D, Rodriguez J, et al. Neonatal lupus erythematosus: 4 cases and clinical review. *Actas Dermosifiliogr.* 2005;96:690–696.
11. Elish D, Silverberg NB. Neonatal lupus erythematosus. *Cutis.* 2006;77(2):82–86.
12. Weston WL, Morelli JG, Lee LA. The clinical spectrum of anti-Ro-positive cutaneous neonatal lupus erythematosus. *J Am Acad Dermatol.* 1999;40(5):675–681.
13. Yu HS, Chiang LC, Chang CH, et al. The cytotoxic effect of neonatal lupus erythematosus and maternal sera on keratinocyte cultures is complement-dependent and can be augmented by ultraviolet irradiation. *Br J Dermatol.* 1996;135(2):297–301.
14. Furukawa F. Antinuclear antibody-keratinocyte interactions in photosensitive cutaneous lupus erythematosus. *Histol Histopathol.* 1999;14(2):627-633.
15. Xue D, Shi H, Smith JD, et al. A lupus-like syndrome develops in mice lacking the Ro 60-kDa protein, a major lupus autoantigen. *Proc Natl Acad Sci U S A.* 2003;100(13): 7503–7508. Epub 2003 Jun 3.
16. Cimaz R, Biggioggero M, Catelli L, et al. Ultraviolet light exposure is not a requirement for the development of cutaneous neonatal lupus. *Lupus.* 2002;11(4):257-260.
17. Lee LA. Transient autoimmunity related to maternal autoantibodies: neonatal lupus. *Autoimmun Rev.* 2005;4:207-213.
18. Buyon JP, Rupel A, Clancy RM. Neonatal lupus syndromes. *Lupus.* 2004;13(9):705-712.
19. Collagen vascular disorders. In: Paller A, Mancini A, eds. *Hurwitz Clinical Pediatric Dermatology: a Textbook of Skin Disorders of Childhood and Adolescence.* 4th ed. Philadelphia, PA: Elsevier Saunders; 2011.
20. Brucato A, Frassi M, Franceschini F, et al. Risk of congenital complete heart block in newborns of mothers with anti-Ro/SSA antibodies detected by counterimmunoelectrophoresis: a prospective study of 100 women. *Arthritis Rheum.* 2001;44:1832–1835.
21. Chunharas A, Nuntnarumit P, Hongeng S, et al. Neonatal lupus erythematosus: clinical manifestations and management. *J Med Assoc Thai.* 2002;85(Suppl 4):S1302–S1308.
22. Laurinaviciene R, Christesen HT, Bygum A. New aspects in the clinical spectrum of neonatal lupus. Eur *J Pediatr.* 2012;171(5):801–805. doi: 10.1007/s00431-011-1618-z. Epub 2011 Nov 22.

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